

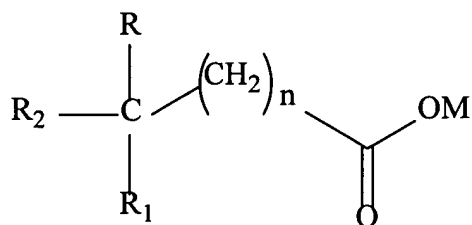
AMENDMENTS TO THE CLAIMS

1. to 27. (Cancelled)

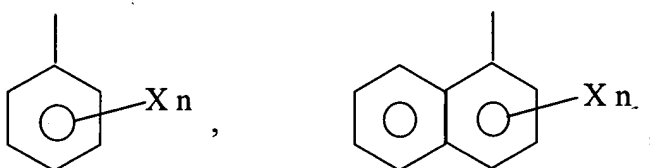
28. **(Currently Amended)** A method of treating a neoplastic disease in a patient in need thereof, wherein the neoplastic disease is selected from the group consisting of: carcinoma of the adrenal gland, carcinoma of the bladder, carcinoma of the breast, high grade glioma, glioblastoma multiforme, anaplastic astrocytoma, low grade astrocytoma, brain stem glioma, primitive neuroectodermal tumors, medulloblastoma, pinealoblastoma, rhabdoid tumor of the central nervous system, oligodendroglioma, mixed glioma, neurofibroma, schwannoma, visual pathway glioma, ependymoma, germ cell tumors, meningioma, carcinoma of the colon, carcinoma of the rectum, carcinoma of the esophagus, primary liver cancer, metastatic liver cancer, carcinoma of the head, carcinoma of the neck, adenocarcinoma of the lung, large cell undifferentiated carcinoma of the lung, bronchio-alveolar carcinoma of the lung, squamous cell carcinoma of the lung, nonsmall cell carcinoma of the lung, non-Hodgkin's lymphoma, chronic leukemia, mesothelioma, malignant melanoma, malignant fibrous histiocytoma, multiple myeloma, neuroblastoma, a neuroendocrine tumor, carcinoma of the ovary, carcinoma of the pancreas, a primitive neuroectodermal tumor outside the central nervous system, adenocarcinoma of the prostate, carcinoma of the kidney, sarcoma, carcinoma of the small intestine, carcinoma of the stomach, carcinoma of the uterus, carcinoma of the vulva, and carcinoma of an unknown primary source;
the method comprising:

administering to a patient first and second pharmaceutical compositions, each at an infusion rate of from about 100 mL/hr to about 400 mL/hr ~~of a pharmaceutical composition,~~

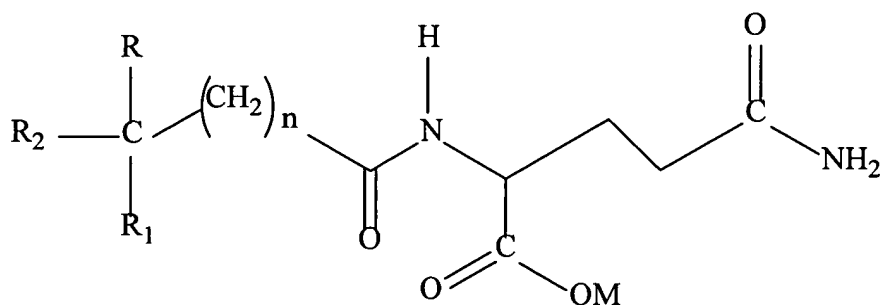
the first pharmaceutical composition comprising an aqueous solution of a compound of Formula IV:



wherein R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II:



wherein X is a halogen, lower alkyl (C₁₋₆), lower alkoxy (C₁₋₆), cycloalkyl, cycloalkoxy, aryl, substituted aryl (C₆₋₁₂) or hydroxy and n is 0, 1, 2, 3, or 4; M is hydrogen, a salt forming cation, alkyl (C₁₋₆), cycloalkyl, or aryl (C₆₋₁₂); and n is 0-5; and, a compound of Formula I:



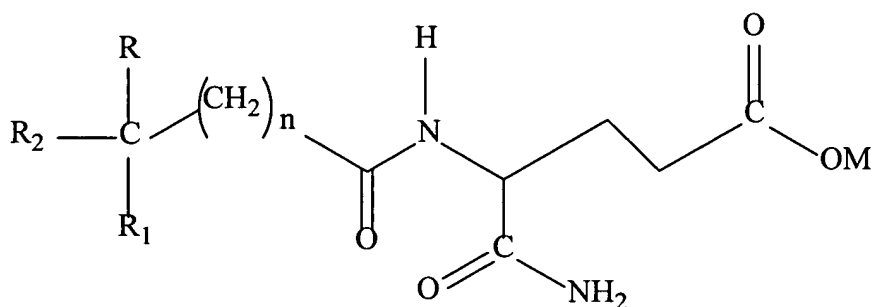
or

wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II;

and a second pharmaceutical composition, comprising a compound of Formula I

wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II; and

a compound of Formula III



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II;

wherein in the first pharmaceutical composition the compound of Formula IV and the compound of Formula I ~~or III~~ are present in a 4:1 ratio by weight, and the combined concentration of the compound of Formula IV and the compound of Formula I ~~or III~~ is from about 70 mg/mL to about 150 mg/mL; and

wherein, in the second pharmaceutical composition, the compound of formula I and the compound of formula III are present in a 4:1 ratio and the combined concentration of the compounds of formula I and formula III is from about 200 mg/mL to about 350 mg/mL.

29. **(Currently Amended)** The method of claim 28, wherein the infusion rate is about 250 mL/hr to about 300 mL/hr, and further comprising performing the administering step sufficiently often to reach a dosage level of from about 0.1 g/kg/day to about 2.6 g/kg/day for the first pharmaceutical composition and from about 0.6 g/kg/day to about 25 g/kg/day for the second pharmaceutical composition.

30. **(Currently Amended)** The method of claim 29, wherein the dosage level is from about 0.2 g/kg/day to about 0.9 g/kg/day for the first pharmaceutical composition and from about 5.0 g/kg/day to about 12.0 g/kg/day for the second pharmaceutical composition.

31. to 47. (Cancelled)

48. **(Currently Amended)** The method of claim 28, wherein in the compound of Formula IV, M is hydrogen or sodium; n is 0; R is H or C₃H₇; R₁ is selected from the group consisting of H, CH₃, CH₃-O-, C₂H₅, and C₃H₇; R₂ is selected from Formula II, wherein X is Cl, F, or OH; and wherein in the ~~compound~~ compounds of Formula I ~~or~~ and III, M is hydrogen or sodium; n is 0; R is H or C₃H₇; R₁ is selected from the group consisting of H, CH₃, CH₃-O-, C₂H₅, and C₃H₇; R₂ is selected from Formula II, wherein X is Cl, F, or OH.

49. **(Currently Amended)** The method of claim 28, wherein the compound of Formula IV is phenylacetic acid or a pharmaceutically acceptable salt thereof, ~~and~~ the compound of Formula I is phenylacetylglutamine or a pharmaceutically acceptable salt thereof, ~~or~~ and the compound of Formula III is phenylacetylisoglutamine or a pharmaceutically acceptable salt thereof.

50. **(Currently Amended)** The method of claim 49, wherein the combined concentration of the compounds of formula IV and formula I in the first pharmaceutical composition ~~or III~~ is about 80 mg/mL.

51. (Previously Presented) The method of claim 28 wherein the pharmaceutical composition comprises a compound of formula I selected from phenylacetylglutamine or a pharmaceutically acceptable salt thereof.

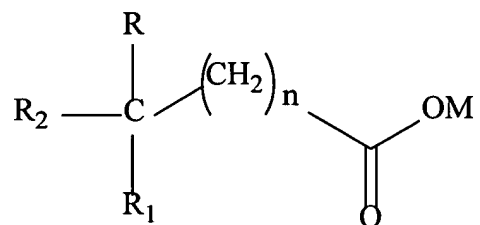
52. (Previously Presented) The method of claim 28 wherein the pharmaceutical comprises a compound of formula III selected from phenylacetylisoglutamine or a pharmaceutically acceptable salt thereof.

53.-54 (Cancelled)

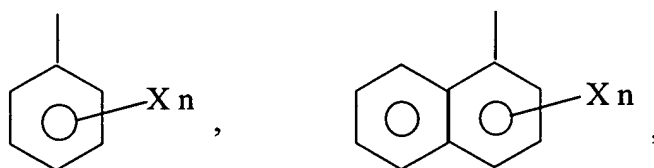
--55. (New) A method of treating a neoplastic disease in a patient in need thereof, wherein the neoplastic disease is selected from the group consisting of: carcinoma of the adrenal gland, carcinoma of the bladder, carcinoma of the breast, high grade glioma, glioblastoma multiforme, anaplastic astrocytoma, low grade astrocytoma, brain stem glioma, primitive neuroectodermal tumors, medulloblastoma, pinealoblastoma, rhabdoid tumor of the central nervous system, oligodendroglioma, mixed glioma, neurofibroma, schwannoma, visual pathway glioma, ependymoma, germ cell tumors, meningioma, carcinoma of the colon, carcinoma of the rectum, carcinoma of the esophagus, primary liver cancer, metastatic liver cancer, carcinoma of the head, carcinoma of the neck, adenocarcinoma of the lung, large cell undifferentiated carcinoma of the lung, bronchio-alveolar carcinoma of the lung, squamous cell carcinoma of the lung, nonsmall cell carcinoma of the lung, non-Hodgkin's lymphoma, chronic leukemia, mesothelioma, malignant melanoma, malignant fibrous histiocytoma, multiple myeloma, neuroblastoma, a neuroendocrine tumor, carcinoma of the ovary, carcinoma of the pancreas, a primitive neuroectodermal tumor outside the central nervous system, adenocarcinoma of the prostate, carcinoma of the kidney, sarcoma, carcinoma of the small intestine, carcinoma of the stomach, carcinoma of the uterus, carcinoma of the vulva, and carcinoma of an unknown primary source; the method comprising:

administering to a patient first and a second pharmaceutical compositions, each composition administered at an infusion rate of from about 100 mL/hr to about 400 mL/hr,

the first pharmaceutical composition comprising an aqueous solution of a compound of Formula IV:

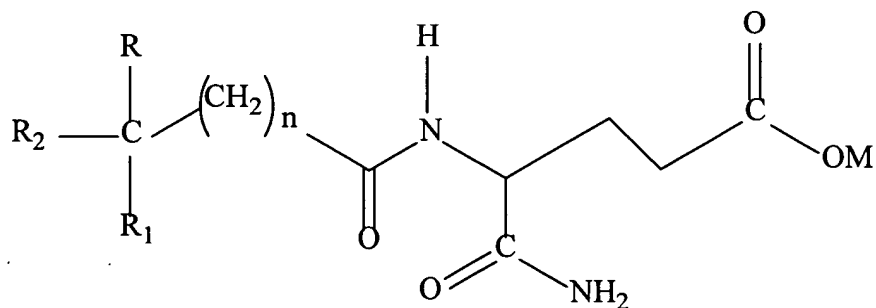


wherein R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II:



wherein X is a halogen, lower alkyl (C₁₋₆), lower alkoxy (C₁₋₆), cycloalkyl, cycloalkoxy, aryl, substituted aryl (C₆₋₁₂) or hydroxy and n is 0, 1, 2, 3, or 4; M is hydrogen, a salt forming cation, alkyl (C₁₋₆), cycloalkyl, or aryl (C₆₋₁₂); and n is 0-5; and,

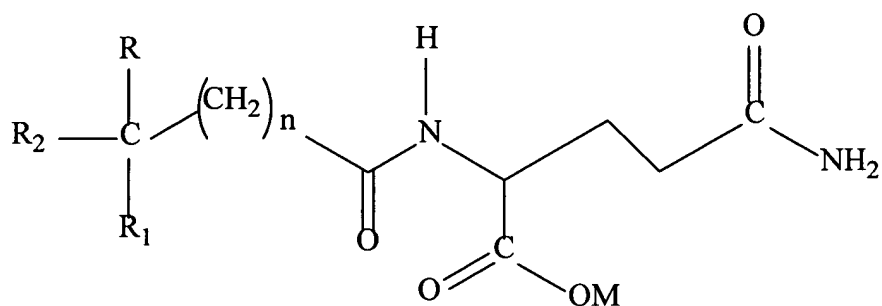
Formula III



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II;

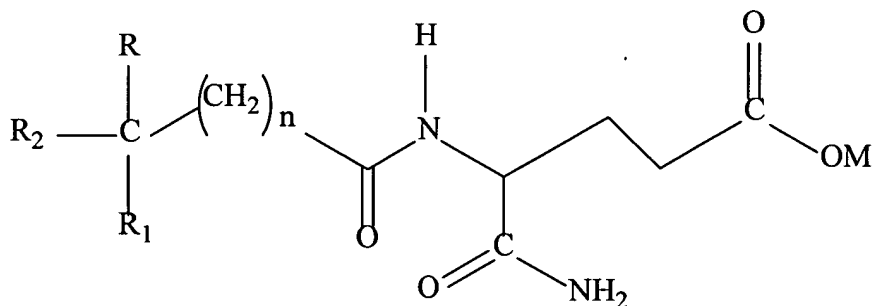
and a second pharmaceutical composition, comprising:

a compound of Formula I:



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II; and

a compound of Formula III



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C₁₋₆), a cycloalkyl, or an aryl (C₆₋₁₂); R and R₁ are independently selected from the group consisting of H, lower alkoxy (C₁₋₆), and lower alkyl (C₁₋₆); R₂ is selected from Formula II;

wherein in the first pharmaceutical composition the compound of Formula IV and the compound of Formula III are present in a 4:1 ratio by weight, and the combined concentration of the compound of Formula IV and the compound of Formula I or III is from about 70 mg/mL to about 150 mg/mL; and

wherein in the second pharmaceutical composition the compound of formula I and the compound of formula III are present in a 4:1 ratio and the combined concentration of the compounds of formula I and formula III is from about 200 mg/mL to about 350 mg/mL.

56. (New) The method of claim 55, wherein the infusion rate is about 250 mL/hr to about 300 mL/hr, and further comprising performing the administering step sufficiently often to reach a dosage level of from about 0.1 g/kg/day to about 2.6 g/kg/day for the first pharmaceutical composition and from about 0.6 g/kg/day to about 25 g/kg/day for the second pharmaceutical composition.

57. (New) The method of claim 56, wherein the dosage level is from about 0.2 g/kg/day to about 0.9 g/kg/day for the first pharmaceutical composition and from about 5.0 g/kg/day to about 12.0 g/kg/day for the second pharmaceutical composition.

58. (New) The method of claim 55, wherein in the compound of Formula IV, M is hydrogen or sodium; n is 0; R is H or C₃H₇; R₁ is selected from the group consisting of H, CH₃, CH₃-O-, C₂H₅, and C₃H₇; R₂ is selected from Formula II, wherein X is Cl, F, or OH; and wherein in the compounds of Formula I and III, M is hydrogen or sodium; n is 0; R is H or C₃H₇; R₁ is selected from the group consisting of H, CH₃, CH₃-O-, C₂H₅, and C₃H₇; R₂ is selected from Formula II, wherein X is Cl, F, or OH.

59. (New) The method of claim 55, wherein the compound of Formula IV is phenylacetic acid or a pharmaceutically acceptable salt thereof, the compound of Formula I is phenylacetylglutamine or a pharmaceutically acceptable salt thereof, and the compound of

Formula III is phenylacetylisoglutamine or a pharmaceutically acceptable salt thereof.

60. (New) The method of claim 59, wherein the combined concentration of the compounds of formula IV and formula III in the first pharmaceutical composition is about 80 mg/mL.

61. (New) The method of claim 55 wherein the compound of formula I selected from phenylacetylglutamine or a pharmaceutically acceptable salt thereof.

62. (New) The method of claim 55 wherein the compound of formula III selected from phenylacetylisoglutamine or a pharmaceutically acceptable salt thereof.--